

DETAILED ACTION

Status of the Claims

1. Claims 49, 56-71, 73-80, 83-84, 86-93, 96-97, 99-102, 122-123, 127-131, 133-134, 137-143 and 146-154 are pending.

Applicants' amendment filed January 15, 2010 is acknowledged. Applicants' response has been fully considered. Claims 49, 60-66, 80, 88-90, 93, 99, 101, 127-129, 148 and 153 have been amended, and claim 98 has been cancelled. Therefore, claims 49, 56-71, 73-80, 83-84, 86-93, 96-97, 99-102, 122-123, 127-131, 133-134, 137-143 and 146-154 are examined.

Withdrawn Claim Objections

2. The previous objection to claim 57 is withdrawn in view of applicants' amendment to the claim in the amendment filed January 15, 2010.

Withdrawn Claim Rejections - 35 USC § 112

3. The previous rejection of claims 49, 60-66, 80, 88, 89, 93, 123, 127-131, 134, 137-141, 148, 153 and 154 under 35 U.S.C. 112, second paragraph is withdrawn in view of applicants' amendment to the claims, and applicants' response at pages 191-193 in the amendment filed January 15, 2010.

Examiner's Amendment

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Alan D. Miller on April 19, 2010.

Examiner's Amendment to the Claims:

Claims 80 and 93 have been amended as follows:

80. (Currently amended) The substrate or the precursor of the substrate of claim 56, wherein the fluorophore comprises a dansyl group, an acridine group, ~~an Alexa-Fluor group,~~ ~~a BODIPY group,~~ ~~an Oregon Green group,~~ ~~a Rhodamine Green group,~~ ~~a Rhodamine Red-X group,~~ ~~a Texas Red group,~~ ~~a Cascade Blue group,~~ ~~a Cascade Yellow group,~~ ~~a Marina Blue group,~~ ~~a Pacific Blue group,~~ ~~an AMCA-X group,~~ a rhodamine group, or a coumarin group.

93. (Currently amended) The chemical compound of claim 90, wherein the fluorophore comprises a dansyl group, an acridine group, ~~an Alexa-Fluor group,~~ ~~a BODIPY group,~~ ~~an Oregon Green group,~~ ~~a Rhodamine Green group,~~ ~~a Rhodamine Red-X group,~~ ~~a Texas Red group,~~ ~~a Cascade Blue group,~~ ~~a Cascade Yellow group,~~ ~~a Marina Blue group,~~ ~~a Pacific Blue group,~~ ~~an AMCA-X group,~~ a rhodamine group, or a coumarin group.

The following is an Examiner's Statement of Reasons for Allowance: The following reference is related to the claimed invention. Nagai *et al.* (Nature Biotechnology 18, 313-316, March 2000) teach a method for visualizing phosphorylation of proteins in living cells using a fluorescent indicator composed of two green fluorescent protein (GFP) variants (i.e., RGFP and BGFP) joined by the kinase inducible domain (KID) of the transcription factor cyclic adenosine monophosphate (cAMP)-responsive element binding protein (CREB), where KID sequence is ART (TSSEILSRPSYRKILNDLSSDT; Fig. 1) or Kempart (TSLRRASLGTGHAVRAIGRLSST; Fig. 1) and where phosphorylation of KID by the cAMP-dependent protein kinase A (PKA) decreased the fluorescence resonance energy transfer (FRET) among the flanking GFPs. However, Nagai *et al.* do not teach a specific substrate for a protein kinase comprising SEQ ID NO:1 (SFRRRR) or 3 (XSFFFFK) and a fluorophore; or a peptide substrate for a protein kinase or a precursor of the substrate comprising a Ser, Thr or Tyr on a terminal end of the peptide, having at least one fluorophore, wherein a fluorophore is attached to the Ser, Thr or Tyr on the terminal end of the peptide, and wherein the fluorophore is attached to the peptide via a specific linker; in case of a precursor of the substrate, a photolabile side chain is attached to the Ser, Thr or Tyr on the terminal end of the peptide. Therefore, the claims are allowable over the art of record.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue

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fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached at 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Chih-Min Kam/

Primary Examiner, Art Unit 1656

CMK

January 19, 2010